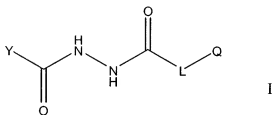


AMENDMENT TO THE CLAIMS

CLAIMS:

1. (Currently amended) A compound having the formula I



wherein

Y is a residue of a macromolecule, wherein the macromolecule is a compound having at least one group that can react with a hydrazide compound, wherein the compound is selected from the group consisting of an oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, a glycolipid, a polysaccharide, a protein, and a synthetic polymer;

Q is a SH group, or is selected from the group consisting of C₁₋₂₄ alkyl halide, C₁₋₂₄ alkoxy-C₁₋₂₄ alkyl, α -halocarbonyl, maleimides, vinyl sulfones, acrylonitriles, α -methylene esters, quinine methides, acryloyl esters, acryloyl amide, α -halo esters and α -halo amides; and

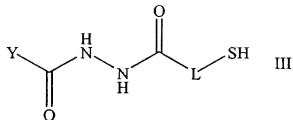
L is a polyalkylene group, a polyether group, a polyamide group, a polyimino group, an aryl group, a polyester, or a polythioether group, wherein when Q is a thiol group, Y is not a residue of hyaluronan.

2. (Original) The compound of claim 1, wherein the macromolecule comprises an oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, a glycolipid, or a pharmaceutically-acceptable compound.
3. (Original) The compound of claim 1, wherein the macromolecule comprises a polysaccharide, a protein, or a synthetic polymer.

4. (Withdrawn) The compound of claim 1, wherein the macromolecule comprises a polysaccharaide, wherein the polysaccharide comprises a sulfated-glycosaminoglycan.
5. (Withdrawn) The compound of claim 4, wherein the polysaccharide comprises chondroitin sulfate, dermatan, heparan, heparin, dermatan sulfate, heparan sulfate, alginic acid, pectin, or carboxymethylcellulose.
6. (Withdrawn) The compound of claim 1, wherein the macromolecule comprises a synthetic polymer, and the synthetic polymer comprises glucuronic acid, polyacrylic acid, polyaspratic acid, polytartaric acid, polyglutamic acid, or polyfumaric acid.
7. (Original) The compound of claim 1, wherein the macromolecule comprises a protein, and the protein comprises a naturally-occurring protein or a recombinant protein.
8. (Original) The compound of claim 1, wherein the macromolecule comprises a protein, and the protein comprises an extracellular matrix protein, a chemically-modified extracellular matrix protein, or a partially hydrolyzed derivative of an extracellular matrix protein.
9. (Original) The compound of claim 8, wherein the protein comprises collagen, elastin, decorin, laminin, or fibronectin.
10. (Withdrawn) The compound of claim 1, wherein Q is a thiol-reactive electrophilic functional group, wherein the thiol-reactive electrophilic functional group comprises an electron-deficient vinyl group.
11. (Withdrawn) The compound of claim 10, wherein the electron-deficient vinyl group comprises a nitro group, a cyano group, an ester group, an aldehyde group, a keto group, a sulfone group, or an amide group.
12. (Withdrawn) The compound of claim 10, wherein the thiol-reactive electrophilic functional group comprises an acrylate group.
13. (Original) The compound of claim 1, wherein L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.

14. (Original) The compound of claim 1, wherein Y is a residue of a protein or polysaccharide, Q is a thiol, and L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.

15. (Withdrawn) A method for coupling two or more thiolated compounds, comprising reacting a first thiolated compound having the formula III



wherein

Y is a residue of a macromolecule, and

L is a polyalkylene group, a polyether group, a polyamide group, a

polyimino group, an aryl group, a polyester, or a polythioether group,

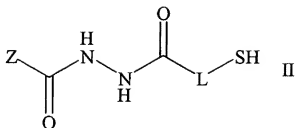
with a second thiolated compound having at least one SH group in the presence of an oxidant,

wherein the first thiolated compound and second thiolated compound are the same or different compounds.

16. (Withdrawn) The method of claim 15, wherein the macromolecule comprises an oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, a glycolipid, or a pharmaceutically-acceptable compound.

17. (Withdrawn) The method of claim 15, wherein the macromolecule comprises a polysaccharide, a protein, or a synthetic polymer.

18. (Withdrawn) The method of claim 15, wherein the macromolecule is a polysaccharide, and the polysaccharide comprises a sulfated-glycosaminoglycan.
19. (Withdrawn) The method of claim 18, wherein the polysaccharide comprises chondroitin sulfate, dermatan, heparan, heparin, dermatan sulfate, heparan sulfate, alginic acid, pectin, or carboxymethylcellulose.
20. (Withdrawn) The method of claim 15, wherein Y is a residue of a polysaccharide or a protein and L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.
21. (Withdrawn) The method of claim 20, wherein the polysaccharide is hyaluronan.
22. (Withdrawn) The method of claim 15, wherein the second thiolated compound is a macromolecule comprising an oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, a glycolipid, or a pharmaceutically-acceptable compound.
23. (Withdrawn) The method of claim 15, wherein the second thiolated compound comprises a polysaccharide having at least one SH group.
24. (Withdrawn) The method of claim 15, wherein the second thiolated compound comprises a sulfated-glycosaminoglycan.
25. (Withdrawn) The method of claim 15, wherein the second thiolated compound comprises chondroitin sulfate, dermatan, heparan, heparin, dermatan sulfate, heparan sulfate, alginic acid, pectin, carboxymethylcellulose, or hyaluronic acid having at least one SH group.
26. (Withdrawn) The method of claim 15 wherein the second thiolated compound comprises a thiolated protein.
27. (Withdrawn) The method of claim 15, wherein the second thiolated compound has the formula II



wherein

Z is a residue of a macromolecule, and

L is a polyalkylene group, a polyether group, a polyamide group, a

polyimino group, an aryl group, a polyester, or a polythioether group.

28. (Withdrawn) The method of claim 27, wherein the macromolecule comprises an oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, a glycolipid, or a pharmaceutically-acceptable compound.

29. (Withdrawn) The method of claim 27, wherein the macromolecule comprises a polysaccharide, a protein, or a synthetic polymer.

30. (Withdrawn) The method of claim 27, wherein Z is a residue of hyaluronan and L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.

31. (Withdrawn) The method of claim 27, wherein Z is a residue of gelatin and L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.

32. (Withdrawn) The method of claim 15, wherein the first thiolated compound and the second thiolated compound are different.

33. (Withdrawn) The method of claim 15, wherein the oxidant comprises a gas comprising oxygen.

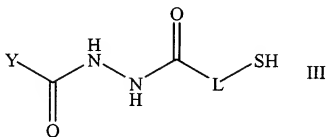
34. (Withdrawn) The method of claim 33, wherein the oxidant further comprises hydrogen peroxide.

35. (Withdrawn) A method for making a compound, comprising reacting

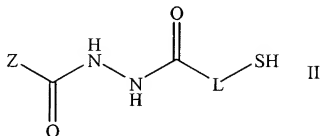
(a) a first thiolated compound comprising a first protein having at least one SH group; and

(b) a second thiolated compound comprising a polysaccharide or synthetic polymer having at least one SH group, in the presence of an oxidant.

36. (Withdrawn) The method of claim 35, wherein the first thiolated compound has the formula III



and the second thiolated compound has the formula II



wherein

Y is a protein residue;

Z is a polysaccharide residue or a residue of a synthetic polymer; and

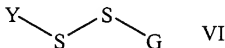
each L is, independently, a polyalkylene group, a polyether group, a polyamide group, a polyester group, a polyimino group, an aryl group, or a polythioether group.

37. (Withdrawn) The method of claim 36, wherein L in formula II and II is, independently, CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.

38. (Withdrawn) The method of claim 36, wherein Z is a residue of hyaluronan.

39. (Withdrawn) A compound made by the method of claim 15.

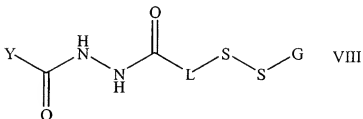
40. (Withdrawn) A compound having at least one fragment comprising the formula VI



wherein Y is a residue of a macromolecule; and

G is a residue of a thiolated compound.

41. (Withdrawn) The compound of claim 40, wherein the fragment comprises the formula VIII



wherein

Y is a residue of a macromolecule, wherein Y is not a residue of hyaluronan;

L is a polyalkylene group, a polyether group, a polyamide group, a polyimino group, an aryl group, a polyester, or a polythioether group; and

G is a residue of a thiolated compound.

42. (Withdrawn) The compound of claim 41, wherein the macromolecule comprises an oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, a glycolipid, or a pharmaceutically-acceptable compound.

43. (Withdrawn) The compound of claim 41, wherein the macromolecule comprises a polysaccharide, a protein, or a synthetic polymer.

44. (Withdrawn) The compound of claim 41, wherein Y is a residue of a sulfated-glycosaminoglycan.

45. (Withdrawn) The compound of claim 41, wherein Y is a residue of chondroitin sulfate, dermatan, heparan, heparin, dermatan sulfate, heparan sulfate, alginic acid, pectin, or carboxymethylcellulose.

46. (Withdrawn) The compound of claim 41, wherein L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.

47. (Withdrawn) The compound of claim 41, wherein G comprises a polysaccharide residue.

48. (Withdrawn) The compound of claim 41, wherein G comprises a sulfated-glycosaminoglycan residue.

49. (Withdrawn) The compound of claim 41, wherein G comprises a residue of chondroitin sulfate, dermatan, heparan, heparin, dermatan sulfate, heparan sulfate, alginic acid, pectin, carboxymethylcellulose, or hyaluronan.

50. (Withdrawn) A method for making a compound, comprising reacting a first thiolated macromolecule having at least one SH group with at least one compound having at least one thiol-reactive electrophilic functional group.

51. (Withdrawn) The method of claim 50, wherein the compound has at least two thiol-reactive electrophilic groups.

52. (Withdrawn) The method of claim 50, wherein the first macromolecule comprises an oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, a glycolipid, a polysaccharide, a protein, a synthetic polymer, or a pharmaceutically-acceptable compound.

53. (Withdrawn) The method of claim 50, wherein the macromolecule comprises a polysaccharide, wherein the polysaccharide comprises a sulfated-glycosaminoglycan.

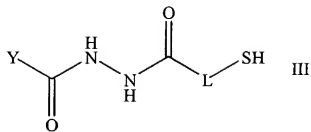
54. (Withdrawn) The method of claim 53, wherein the polysaccharide comprises chondroitin sulfate, dermatan, heparan, heparin, dermatan sulfate, heparan sulfate, alginic acid, pectin, or carboxymethylcellulose.

55. (Withdrawn) The method of claim 53, wherein the polysaccharide comprises hyaluronan.

56. (Withdrawn) The method of claim 50, wherein the macromolecule comprises a protein, wherein the protein comprises an extracellular matrix protein, a partially hydrolyzed extracellular matrix protein, or a chemically-modified extracellular matrix protein.

57. (Withdrawn) The method of claim 56, wherein the protein comprises collagen, elastin, decorin, laminin, or fibronectin.

58. (Withdrawn) The method of claim 50, wherein the first macromolecule has the formula
III



wherein Y is a residue of a macromolecule, and

L is a polyalkylene group, a polyether group, a polyamide group,

a polyimino group, a polyester, an aryl group, or a polythioether group.

59. (Withdrawn) The method of claim 58, wherein Y is a residue of a polysaccharide or a protein.

60. (Withdrawn) The method of claim 58, wherein Y is a residue of hyaluronan and L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.

61. (Withdrawn) The method of claim 50, further comprising a second thiolated macromolecule, wherein the first and second macromolecule are the same or different.

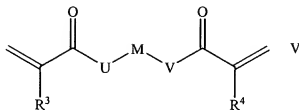
62. (Withdrawn) The method of claim 50, wherein the thiol-reactive electrophilic functional group comprises an electron-deficient vinyl group.

63. (Withdrawn) The method of claim 62, wherein the electron-deficient vinyl group comprises a nitro group, a cyano group, an ester group, an aldehyde group, a keto group, a sulfone group, or an amide group.

64. (Withdrawn) The method of claim 50, wherein the compound has two electron-deficient vinyl groups, wherein the two electron-deficient vinyl groups are the same.

65. (Withdrawn) The method of claim 50, wherein the compound comprises a diacrylate, a dimethacrylate, a diacrylamide, a dimethacrylamide, or a combination thereof.

66. (Withdrawn) The method of claim 50, wherein the compound has the formula V



wherein R^3 and R^4 are, independently, hydrogen or lower alkyl;

U and V are, independently, O or NR^5 , wherein R^5 is, independently, hydrogen or lower alkyl; and

M is a polyalkylene group, a polyether group, a polyamide group, a polyimino group, a polyester, an aryl group, or a polythioether group.

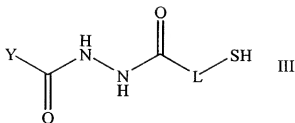
67. (Withdrawn) The method of claim 66, wherein R^3 and R^4 are hydrogen, U and V are oxygen, and M is a polyether group.

68. (Withdrawn) The method of claim 66, wherein R^3 and R^4 are hydrogen, U and V are NH, and M is a polyether group.

69. (Withdrawn) The method of claim 66, wherein R^3 and R^4 are methyl, U and V are oxygen, and M is a polyether group.

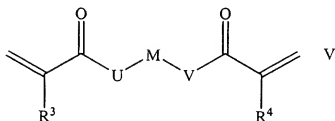
70. (Withdrawn) The method of claim 66, wherein R^3 and R^4 are methyl, U and V are NH, and M is a polyether group.

71. (Withdrawn) The method of claim 50, wherein the first thiolated macromolecule has the formula III



wherein Y is a residue of polysaccharide, and

L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$, and the compound has the formula V



wherein R^3 and R^4 are, independently, hydrogen or lower alkyl;

U and V are, independently, O or NR^5 , wherein R^5 is, independently, hydrogen or lower alkyl; and

M is a polyether group.

72. (Withdrawn) The method of claim 71, wherein Y is a residue of hyaluronan, and the reaction further comprises reacting gelatin having at least one thiol group with the compound having the formula V.

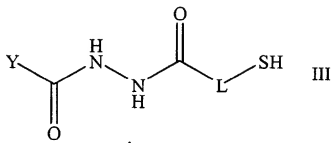
73. (Withdrawn) The method of claim 71, wherein the polysaccharide comprises a first polysaccharide and second polysaccharide having the formula I, wherein in the first polysaccharide, Y is a residue of a first sulfated-glycosaminoglycan, and in the second polysaccharide, Y is a residue of a second sulfated-glycosaminoglycan, wherein the first and second sulfated-glycosaminoglycans are the same or different.

74. (Withdrawn) The method of claim 71, wherein the polysaccharide comprises a first polysaccharide and second polysaccharide having the formula I, wherein in the first polysaccharide, Y is a residue of hyaluronan, and in the second polysaccharide, Y is a residue of a sulfated-glycosaminoglycan.

75. (Withdrawn) The method of claim 71, further comprising reacting a protein, an extracellular matrix, or growth factor having at least one thiol group with the compound having the formula V.

76. (Withdrawn) The method of claim 75, wherein the polysaccharide comprises a sulfated-glycosaminoglycan.

77. (Withdrawn) The method of claim 50, wherein the first thiolated macromolecule has the formula III

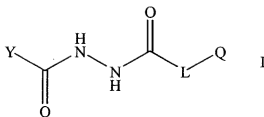


wherein Y is a residue of polysaccharide, and

L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$, and the compound is mitomycin C modified with an acrylate group.

78. (Withdrawn) A method for making a compound, comprising reacting a thiolated macromolecule having at least one thiol-reactive electrophilic functional group with at least one compound having at least two thiol groups.

79. (Withdrawn) The method of claim 78, wherein the first thiolated macromolecule has the formula I

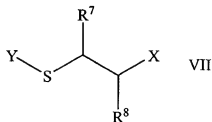


wherein Y is a residue of the macromolecule;

Q is the thiol-reactive electrophilic functional group; and

L is a polyalkylene group, a polyether group, a polyamide group, a polyimino group, a polyester, an aryl group, or a polythioether group.

80. (Withdrawn) The method of claim 79, wherein Y is a residue of a polysaccharide.
81. (Withdrawn) The method of claim 79, wherein Y is hyaluronan and L is CH₂CH₂ or CH₂CH₂CH₂.
82. (Withdrawn) The compound produced by the process of claim 50.
83. (Withdrawn) A compound having at least one fragment comprising the formula VII



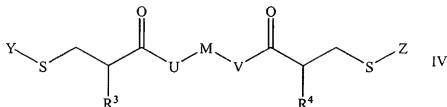
wherein R⁷ and R⁸ are, independently, hydrogen or lower alkyl;

X is an electron-withdrawing group; and

Y is a residue of a macromolecule.

84. (Withdrawn) The compound of claim 83, wherein Y is a polysaccharide residue.

85. (Withdrawn) The compound of claim 83, wherein the fragment comprises the formula IV



wherein R³ and R⁴ are, independently, hydrogen or lower alkyl;

U and V are, independently, O or NR⁵, wherein R⁵ is, independently,

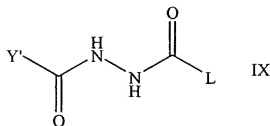
hydrogen or lower alkyl;

Y is a residue of a protein;

Z is a polysaccharide residue or a residue of synthetic polymer; and

M is a polyalkylene group, a polyether group, a polyamide group, a polyester group, a polyimino group, an aryl group, or a polythioether group.

86. (Withdrawn) The compound of claim 85, wherein Y has the formula IX



wherein Y' is a residue of the first protein;

L is a polyalkylene group, a polyether group, a polyamide group,

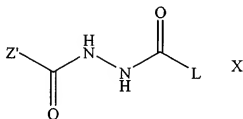
a polyester group, a polyimino group, an aryl group, or a polythioether group,

wherein the L group is covalently bonded to the sulfur atom.

87. (Withdrawn) The compound of claim 86, wherein the protein comprises an extracellular matrix protein, a partially hydrolyzed extracellular matrix protein, or a chemically-modified extracellular matrix protein.

88. (Withdrawn) The compound of claim 86, wherein the protein comprises collagen, elastin, decorin, laminin, or fibronectin.

89. (Withdrawn) The compound of claim 85, wherein Z has the formula X



wherein Z' is a polysaccharide residue or a residue of a synthetic polymer; and

L is a polyalkylene group, a polyether group, a polyamide group, a polyester group,

a polyimino group, an aryl group, or a polythioether group,

wherein the L group is covalently bonded to the sulfur atom.

90. (Withdrawn) The compound of claim 89, wherein Z is a residue of hyaluronan or chondroitin sulfate and L is CH_2CH_2 or $\text{CH}_2\text{CH}_2\text{CH}_2$.

91. (Withdrawn) A pharmaceutical composition comprising a pharmaceutically-acceptable compound and the compound of claim 40.

92. (Withdrawn) A pharmaceutical composition comprising a living cell and the compound of claim 40.

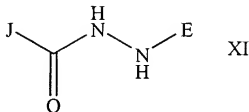
93. (Withdrawn) A method for improving wound healing in a subject in need of such improvement, comprising contacting the wound of the subject with the compound of claim 40.

94. (Withdrawn) A method for delivering at least one pharmaceutically-acceptable compound to a patient in need of such delivery, comprising contacting at least one tissue capable of receiving the pharmaceutically-acceptable compound with the composition of claim 91.

95. (Withdrawn) A method for delivering living cells to a patient in need of such delivery, comprising contacting at least one tissue capable of receiving the living cells with the composition of claim 92.

96. (Withdrawn) The use of the compound of claim 40 as a growth factor, an anti-inflammatory agent, an anti-cancer agent, an analgesic, an anti-infection agent, or an anti-cell attachment agent.

97. (Withdrawn) A compound having the formula XI



wherein J comprises a protein residue; and

E comprises a fluorescent tag, a radiolabel, a targeting moiety, a lipid, a peptide, a radionuclide chelator with a radionuclide, a spin-label, a PEG camouflage, a metal surface, a glass surface, a plastic surface, or a combination thereof.

98. (Withdrawn) The compound of claim 97, wherein the macromolecule comprises a protein, and the protein comprises a naturally-occurring protein or a recombinant protein.

99. (Withdrawn) The compound of claim 97, wherein the protein comprises an extracellular matrix protein, a partially hydrolyzed extracellular matrix protein, or a chemically-modified extracellular matrix protein.

100. (Withdrawn) The compound of claim 97, wherein the protein comprises collagen, elastin, decorin, laminin, or fibronectin.

101. (Withdrawn) A compound produced by the process comprising reacting

- (1) a protein having at least one hydrazide-reactive group and
- (2) a compound having at least one hydrazide group.

102. (Withdrawn) A compound produced by the process comprising reacting

- (1) a protein having at least one hydrazide group and
- (2) a compound having at least one hydrazide-reactive group.

103. (Withdrawn) A pharmaceutical composition comprising a pharmaceutically-acceptable compound and the compound of claim 97.

104. (Withdrawn) A method for improving wound healing in a subject in need of such improvement, comprising contacting the wound of the subject with the compound of claim 97.

105. (Withdrawn) A method for delivering at least one pharmaceutically-acceptable compound to a patient in need of such delivery, comprising contacting at least one tissue capable of receiving the pharmaceutically-acceptable compound with the composition of claim 104.

106. (Withdrawn) The use of the compound of claim 97 as a growth factor, an anti-inflammatory agent, an anti-cancer agent, an analgesic, an anti-infection agent, or an anti-cell attachment agent.

107. (Withdrawn) A kit comprising

- (1) a compound comprising at least one hydrazide group;
- (2) a condensing agent;
- (3) a buffer reagent; and
- (4) a purification column.

108. (Withdrawn) A pharmaceutical composition comprising a pharmaceutically-acceptable compound and the compound of claim 82.

109. (Withdrawn) A pharmaceutical composition comprising a pharmaceutically-acceptable compound and the compound of claim 83.

110. (Withdrawn) A pharmaceutical composition comprising a living cell and the compound of claim 82.

111. (Withdrawn) A pharmaceutical composition comprising a living cell and the compound of claim 83.

112. (Withdrawn) A method for improving wound healing in a subject in need of such improvement, comprising contacting the wound of the subject with the compound of claim 82.

113. (Withdrawn) A method for improving wound healing in a subject in need of such improvement, comprising contacting the wound of the subject with the compound of claim 83.

114. (Withdrawn) The use of the compound of claim 82 as a growth factor, an anti-inflammatory agent, an anti-cancer agent, an analgesic, an anti-infection agent, or an anti-cell attachment agent.

115. (Withdrawn) The use of the compound of claim 83 as a growth factor, an anti-inflammatory agent, an anti-cancer agent, an analgesic, an anti-infection agent, or an anti-cell attachment agent.